AD-A262 807

[...]TATION PAGE

Form Approved
OMB No. 0704-0188

(2)

1. AGENCY USE ONLY (Leave blank)

2. REPORT DATE
Dec 1992

3. REPORT TYPE AND DATES COVERED
Final, N/A

4. TITLE AND SUBTITLE
Relationship between functional residual capacity to various body measurements in normal sheep

5. FUNDING NUMBERS

6. AUTHOR(S)
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8. PERFORMING ORGANIZATION REPORT NUMBER
N/A

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
Department of Respiratory Research (SGRD-UWH-E)
Division of Medicine
Walter Reed Army Institute of Research
Washington, D.C. 20307-5100

10. SPONSORING/MONITORING AGENCY REPORT NUMBER
N/A

11. SUPPLEMENTARY NOTES
N/A

12a. DISTRIBUTION/AVAILABILITY STATEMENT
UNCLASSIFIED/UNLIMITED

12b. DISTRIBUTION CODE
N/A

13. ABSTRACT *(Maximum 200 words)*

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14. SUBJECT TERMS
sheep, functional residual capacity (FRC)

15. NUMBER OF PAGES
4

16. PRICE CODE
N/A

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
UNCLASSIFIED	UNCLASSIFIED	UNCLASSIFIED	UNLIMITED

WR-28-93

Laboratory Animal Science

93-06774

Vol 42, No 6
December 1992

Relationship of Functional Residual Capacity to Various Body Measurements in Normal Sheep

Thomas G. Mundie, Kenneth T. Dodd, and Michael Lagutchik

Abstract | Functional residual capacity (FRC) was determined by nitrogen washout in 55 normal sheep. Data on various external body measurements were collected which included body weight, chest circumference, chest width, body length, height, and sternum length. In addition, data on wet lung weight and wet lung weight/body weight ratio were collected on 10 of the sheep. A significant correlation was found between FRC and all measured parameters except height and sternum length. Multiple linear regression of all external body measurements showed the best correlation of FRC to body weight and body length, while the addition of chest circumference and/or chest width did not significantly improve the correlation. Significant deviation from the population was noted in three sheep (5.5%) that had lung weight/body weight ratios which were significantly lower than the rest of the population.

Functional residual capacity (FRC) is the volume of air in the lung at the end of a normal breath It is the point at which the elastic recoil of the lungs and the chest wall balance one another. Normal FRC may be altered by several disease states or ventilatory support methods. Sheep are being used increasingly in investigations of pulmonary function when direct determination of FRC is impossible and an estimation of FRC is needed. Normal FRC values for sheep have been reported in liters (1), however, to our knowledge, no equation for estimating FRC from weight or other body measurements has been reported. We sought to determine the relationship of FRC to various external body measurements, as well as to lung weight for the range of animal sizes used in laboratory studies and to establish a method of estimating FRC from external body measurements.

Materials and Methods

Fifty-five normal, Q-fever negative, mixed-breed, adult female sheep *(Ovis aries)* (21 to 56 kg) were acquired from a commercial source. All sheep were dewormed and quarantined for 3 weeks. They were housed indoors and feeding was maintained with standard sheep feed supplemented with hay. The sheep were closely shorn for external body measurements. The study protocol was approved by the Institutional Animal Care and Use Committee of the Walter Reed Army Institute of Research. During the conduct of the research described herein, animals were used according to established guidelines (2).

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After administration of topical anesthesia (Cetacaine spray), each animal was intubated transnasally with a cuffed endotracheal tube (custom 40 cm long, 7.5 mm silicon, Bivona, Gary, IN) using a fiberoptic bronchoscope. The endotracheal tube was secured in place by role gauze. Sheep were allowed to stand in a metabolic cage but their heads were restrained by a muzzle and vertical padded bars. Before FRC determination, each animal was acclimated to the restraint and allowed to stand undisturbed in the metabolic cage for several minutes to attain resting ventilatory parameters. The process of intubation, FRC determination, and extubation took no more than 30 minutes. If animals became agitated or began to hyperventilate, they were not used. Neither food nor water were withheld from the sheep before experimentation.

The following external body measurements were made on the sheep while in the standing position. Body weight (WT) was measured using a digital floor scale: body length from the base of the tail to the nose (LGTH), following the contour of the dorsal aspect of the body measured using a cloth yardstick; height (HT) measured at mid-chest level; chest circumference (CIRCUM) measured at the end of exhalation at the level of the Xiphoid process so as not to get significant contribution from abdominal contents; chest width (WDTH) measured dorsal/ventral at the widest portion of the rib cage using X-ray calipers. While the sheep was in dorsal recumbency, the sternum length (STERNUM) was measured from the distal tip of Manubrium to the distal tip of the Xiphoid process. In addition to these external body measurements, wet lung weight (LUNG-WT) and wet lung weight/body weight ratio (LWT/BWT) were determined in 10 sheep as part of a control necropsy in other studies. Necropsy results indicated no evidence of lung injury or abnormalities.

FRC was determined by the nitrogen washout method as originally described by Darling *et al.* (3). Respiratory flow

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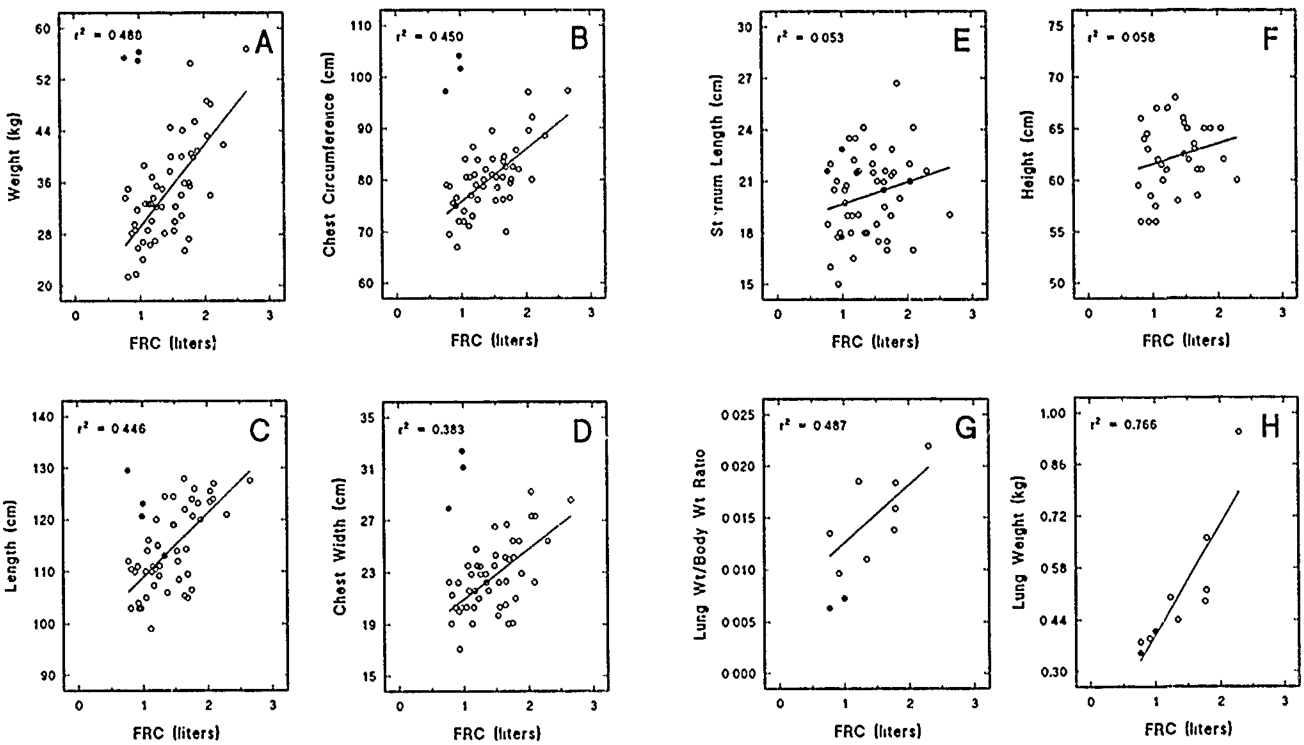

Figure 1. (A) Relationship of functional residual capacity (FRC) to various body measurements including body weight, (B) chest circumference, (C) body length, (D) chest width, (E) sternum length, (F) height, (G) lung weight/body weight ratio, (H) lung weight Dark circles represent data points excluded from by Andrews' sine regression weighing procedures.

was measured using a heated pneumotachometer (Model 3500, Hans Rudolf, Inc., Kansas City, MO). Inspired and expired flow was directed using a large two-way nonrebreathing valve (Model 3813, Hans Rudolf, Inc.). On the inspired side a manual three-way directional stopcock valve directed inspired air from either room air or 100% O_2. On the expired side, a similar 3-way valve directed expired air to either room air or a 40-liter collection bag. Air was sampled proximal to the pneumotachometer for analysis of N_2 concentration (FN_2) using a mass spectrometer. The above described circuit was similar to previously described methods (4). Respiratory flow and FN_2 data were collected into a PC-based data acquisition system (CODAS, DATAQ, Inc., Akron, OH). The expired flow signal was integrated to yield expired volume. The sheep was attached to the breathing apparatus and allowed to breath room air for several minutes. At end expiration, both three-way valves were switched so that the sheep was inspiring 100% O_2 and expiring into the collection bag. FN_2 was monitored until the peak expired concentration was <5%, at which time the valves were returned to room-air breathing. FRC was calculated using the following equation (4):

$$\text{FRC} = \frac{\%N_2(\text{final}) \times \text{Expired Volume} - N_2(\text{tissue})}{\%N_2(\text{alveolar 1}) - \%N_2(\text{alveolar 2})}$$

where,

$\%N_2$(final)	=	Concentration of N_2 in the volume expired
$\%N_2$(alveolar 1)	=	Fraction of N_2 in the alveolar gas initially
$\%N_2$(alveolar 2)	=	Fraction of N_2 in the alveolar gas at the end
N_2(tissue)	=	Volume of N_2 washed out of the blood/tissues (40 ml/min/kg).

Separate linear regressions were performed on each measurement parameter related to FRC and the correlation coefficient (r^2) was determined. The level of significance of the linear regression was determined by a hypothesis test of the slope of the regression line. Significance was accepted at $P < 0.05$. In addition, multiple linear regression was performed on WT, LGTH, CIRCUM, WDTH. Andrews' sine robust regression weighing procedure was used to detect and exclude outlying data points. Once these outliers were excluded, multiple linear regression was performed without weighing.

Results

The relationship of FRC to various body measurements is shown in Figure 1 (Panels A–H). A statistically significant correlation ($P < 0.05$) was found between FRC and WT (r^2 = 0.488), LGTH (r^2 = 0.446), CIRCUM (r^2 = 0.450), WDTH (r^2 = 0.383), LUNG-WT (r^2 = 0.766) and LWT/BWT (r^2 = 0.487), but not between FRC and HT (r^2 = 0.058) or STERNUM (r^2 = 0.053). FRC correlated best with LUNG-WT and can be estimated from the equation:

FRC (liters) = (3.34 * LUNG-WT (kg)) - 0.33.

Multiple linear regression of external body measurements WT, LGTH, CIRCUM, and WDTH showed that FRC can best be estimated from WT and LGTH using the following equation:

FRC (liters)= (0.0271 * WT (kg)) + (0.0168 * LGTH (cm)) - 1.4067

where, $r^2 = 0.536$.

Addition of CIRCUM and WDTH to the multiple regression equation did not significantly improve the correlation coefficient ($r^2 = 0.538$). The external body measurements of three sheep (solid circles in Figure 1) did not correlate well with FRC. Andrews' sine regression weighing procedures were used to exclude these data from all linear regressions (Panels A–G) except the linear regression of LUNG-WT (Panel H).

Discussion

Nitrogen washout determination of FRC in normal sheep was relatively uncomplicated and easily tolerated by most sheep. No significant problems were observed. For male and female adult humans, FRC has been most closely correlated with height but has also been estimated from a combination of height, weight, age and/or body surface area (4–8). In our study of sheep, the best correlation of FRC and external measurements was found with weight and length (equivalent to height in humans). For most of the sheep tested in this study, FRC was found to be significantly correlated with body weight, length, chest circumference, and chest width. It was expected that FRC in normal sheep would correlate with those body measurements which are associated with lung/chest size and not correlate with those parameters which are independent of lung/chest size. Three animals deviated significantly from the population. They had low lung weight/body weight ratios so that there was little correlation with most external body measurements but good correlation with lung weight. The wet lung weight/body weight ratio was significantly lower that the rest of the population.

Table 1 shows FRC and body weight data from this and other studies which have included control FRC data for sheep (8–17). The FRC data reported here are in general agreement with previously reported values for female sheep. The two studies with the lowest FRC data (10, 18) were both conducted using the He dilution method. While most reported studies were conducted using the plethysmographic technique, the nitrogen washout data in our study were comparable. There is not an accepted standard method for determining FRC in spontaneously breathing animals. In fact, there are advantages and disadvantages to all three of these methods.

While the data from this study showed statistically significant correlations between FRC and several external body measurements, there was considerable variation among the animals. The external body measurements used in this study could not be used to predict FRC with an acceptable degree of accuracy for an individual subject. However, these data are useful for estimating FRC from body weight and length.

Table 1. Comparison data for functional residual capacity (FRC) and sheep body weight

Weight[a]	FRC (liters)	FRC (ml/kg)	Method[b]	Reference
35.9	1.41	39.2	N_2	present study
37	1.18	31.9	TGV	8
60	1.40	23.3	He	9
40	1.14	28.5	TGV	10
32	1.00	31.3	TGV	11
24.5	1.11	45.3	TGV	12
34	1.40	41.2	TGV	13
40	1.77	44.3	TGV	14
35	1.31	37.4	TGV	15
35	1.35	38.6	TGV	16
29.2	0.75	25.7	He	17

[a]Sheep body weight reported as mean or median value.
[b]Method of FRC determination. N_2 = Nitrogen washout, He = Helium rebreathing, TGV = thoracic gas volume, plethysmography.

The views of the authors do not reflect the position of the Walter Reed Army Institute of Research, the Walter Reed Army Medical Center, the Department of the Army, or the Department of Defense.

References

1. **Hecker, J. F.** 1986. Respiratory system, p. 38–40. *In* J. F. Hecker (ed.), The sheep as an experimental animal Academic Press, Inc., New York, NY.
2. **National Research Council.** 1985. Guide for the care and use of laboratory animals. NIH Publication No.85-23. Public Health Service, Bethesda, MD.
3. **Darling, R. C., A. Cournand, and D. W. Richards.** 1940 Studies on the intrapulmonary mixture of gases. III An open-circuit method for measuring residual air. J. Clin. Invest. 19:609–618.
4. **Ruppel, G.** 1986. Manual of pulmonary function testing, p. 4–6. C. V. Mosby Company, St. Louis, MO.
5. **Boren, H. G., R. C. Kory, and J. C. Syner.** 1966 The Veterans Administration – Army cooperative study of pulmonary function. Part II. The lung volume and its subdivisions in normal men. Am. J. Med. 41:96–102.
6. **Grimby, G., and B. Soderholm.** 1963. Spirometric studies in normal subjects. Part III. Static lung volumes and maximum voluntary ventilation in adults with a note on physical fitness. Acta Med. Scand. 173:199–205.
7. **Goldman, H. I., and M. R. Becklake.** 1959. Respiratory function tests. Normal values at median altitudes and the prediction of normal results. Am. Rev. Resp. Dis. 79.457–463.
8. **Needham, C. D., M. C. Rogan, and A. McDonald.** 1954. Normal standards for lung volumes, intrapulmonary gas mixing, and maximum breathing capacity. Thorax 9:313–320.
9. **Hutchison, A. A., K. L. Brigham, and J. A. Snapper.** 1982. Effect of histamine on lung mechanics in sheep. Comparison of aerosol and parenteral administration. Am. Rev. Resp. Dis. 126:1025–1029.
10. **Bosse, J., R. Boileau, R. Begin, *et al.*** 1987. Chronic allergic airway disease in the sheep model: functional and lung lavage features. J. Allergy Clin. Immunol. 79:339–344.
11. **Ahmed, T., P. Eyre, A. J. Januszkiewicz, *et al.*** 1980. Role of H_1- and H_2-receptors in airway reactions to histamine in conscious sheep. J. Appl. Physiol. 49:826–833.
12. **Abraham, W. M., A. J. Januskiewitz, M. Mingle, *et al.*** 1980. Sensitivity of bronchoprovocation and tracheal mucous velocity in detecting airway responses to O_3. J. Appl. Physiol. 48:789–793.

13. **Wanner, A., and M. E. Reinhart.** 1978. Respiratory mechanics in conscious sheep. response to methacholine. J. Appl. Physiol. 44:479–482.
14. **Fukushima, M., L. S. King, K. Kang, *et al.*** 1990. Lung mechanics and airway reactivity in sheep during development of oxygen toxicity. J. Appl. Physiol. 69:1779–1785.
15. **Dyer, E. L., and J. R. Snapper.** 1986. Role of circulating granulocytes in sheep lung injury produced by phorbol myristate acetate. J. Appl. Physiol. 60:576–589.
16. **Wheeler, A. P., G. Jesmok, and K. L. Brigham.** 1990 Tumor necrosis factor's effects on lung mechanics, gas exchange, and airway reactivity in sheep. J. Appl. Physiol. 68:2542–2549.
17. **Wanner, A., R. J. Mezey, M. E. Reinhart, *et al.*** 1979 Antigen-induced bronchospasm in conscious sheep. J Appl Physiol. 47:917–922.
18. **Begin, R., M. Rola-Pleszczynski, and P. Sirios.** 1981 Sequential analysis of the bronchoalveolar milieu in conscious sheep. J. Appl. Physiol. 50:665–671.